

External links

- *Fast Fourier Transforms* ^[16], Connexions online book edited by C. Sidney Burrus, with chapters by C. Sidney Burrus, Ivan Selesnick, Markus Pueschel, Matteo Frigo, and Steven G. Johnson (2008).
- Links to FFT code and information online. ^[17]
- National Taiwan University - FFT ^[18]
- FFT programming in C++ — Cooley–Tukey algorithm. ^[19]
- Online documentation, links, book, and code. ^[20]
- Using FFT to construct aggregate probability distributions ^[21]
- Sri Welaratna, "30 years of FFT Analyzers ^[22]", *Sound and Vibration* (January 1997, 30th anniversary issue). A historical review of hardware FFT devices.
- FFT Basics and Case Study Using Multi-Instrument ^[23]
- FFT Textbook notes, PPTs ^[24] at Holistic Numerical Methods Institute.
- ALGLIB FFT Code ^[25] GPL Licensed multilanguage (VBA, C++, Pascal, etc.) numerical analysis and data processing library.

References

- [1] <http://www.math.ohiou.edu/~mjm/research/libftsh.html>
- [2] <http://ieeexplore.ieee.org/search/wrapper.jsp?arnumber=1162805>
- [3] <http://fftw.org/fftw-paper-ieee.pdf>
- [4] http://ieeexplore.ieee.org/xpls/abs_all.jsp?arnumber=1162257
- [5] http://ieeexplore.ieee.org/xpl/freeabs_all.jsp?arnumber=1164785
- [6] <http://www.fftw.org/newsplit.pdf>
- [7] <http://dx.doi.org/10.1007/BF01261607>
- [8] <http://www.math.ohiou.edu/~mjm/research/MOHLEN1999P.pdf>
- [9] <http://www.tu-chemnitz.de/~potts/paper/ndft.pdf>
- [10] <http://pantheon.yale.edu/~mwt7/sph2.pdf>
- [11] <http://portal.acm.org/citation.cfm?id=240432>
- [12] <http://ieeexplore.ieee.org/search/wrapper.jsp?arnumber=1165220>
- [13] <http://ieeexplore.ieee.org/search/wrapper.jsp?arnumber=1165284>
- [14] <http://ieeexplore.ieee.org/search/wrapper.jsp?arnumber=1162035>
- [15] <http://www.jstor.org/view/00255718/di970565/97p0015m/0>
- [16] <http://cnx.org/content/col10550/>
- [17] <http://www.fftw.org/links.html>
- [18] <http://www.cmlab.csie.ntu.edu.tw/cml/dsp/training/coding/transform/fft.html>
- [19] <http://www.librow.com/articles/article-10>
- [20] <http://www.jjj.de/fxt/>
- [21] http://www.vosesoftware.com/ModelRiskHelp/index.htm#Aggregate_distributions/Aggregate_modeling_-_Fast_Fourier_Transform_FFT_method.htm
- [22] <http://www.dataphysics.com/support/library/downloads/articles/DP-30%20Years%20of%20FFT.pdf>
- [23] http://www.multi-instrument.com/doc/D1002/FFT_Basics_and_Case_Study_using_Multi-Instrument_D1002.pdf
- [24] <http://numericalmethods.eng.usf.edu/topics/fft.html>
- [25] <http://www.alglib.net/fasttransforms/fft.php>

Fourier transform spectroscopy

Fourier transform spectroscopy is a measurement technique whereby spectra are collected based on measurements of the coherence of a radiative source, using time-domain or space-domain measurements of the electromagnetic radiation or other type of radiation. It can be applied to a variety of types of spectroscopy including optical spectroscopy, infrared spectroscopy (FTIR, FT-NIRS), nuclear magnetic resonance (NMR) and magnetic resonance spectroscopic imaging (MRSI)^[1], mass spectrometry and electron spin resonance spectroscopy. There are several methods for measuring the temporal coherence of the light, including the continuous wave *Michelson* or *Fourier transform* spectrometer and the pulsed Fourier transform spectrograph (which is more sensitive and has a much shorter sampling time than conventional spectroscopic techniques, but is only applicable in a laboratory environment).

The term *Fourier transform spectroscopy* reflects the fact that in all these techniques, a Fourier transform is required to turn the raw data into the actual spectrum.

Conceptual introduction

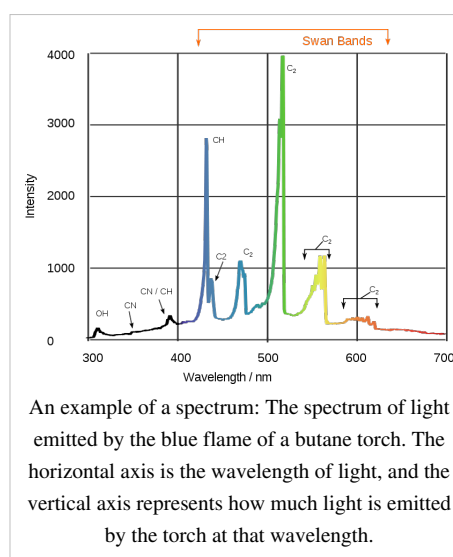
Measuring an emission spectrum

One of the most basic tasks in spectroscopy is to characterize the spectrum of a light source: How much light is emitted at each different wavelength. The most straightforward way to measure a spectrum is to pass the light through a monochromator, an instrument that blocks all of the light *except* the light at a certain wavelength (the un-blocked wavelength is set by a knob on the monochromator). Then the intensity of this remaining (single-wavelength) light is measured. The measured intensity directly indicates how much light is emitted at that wavelength. By varying the monochromator's wavelength setting, the full spectrum can be measured. This simple scheme in fact describes how *some* spectrometers work.

Fourier transform spectroscopy is a less intuitive way to get the same information. Rather than allowing only one wavelength at a time to pass through to the detector, this technique lets through a beam containing many different wavelengths of light at once, and measures the *total* beam intensity. Next, the beam is modified to contain a *different* combination of wavelengths, giving a second data point. This process is repeated many times. Afterwards, a computer takes all this data and works backwards to infer how much light there is at each wavelength.

To be more specific, between the light source and the detector, there is a certain configuration of mirrors that allows some wavelengths to pass through but blocks others (due to wave interference). The beam is modified for each new data point by moving one of the mirrors; this changes the set of wavelengths that can pass through.

As mentioned, computer processing is required to turn the raw data (light intensity for each mirror position) into the desired result (light intensity for each wavelength). The processing required turns out to be a common algorithm called the Fourier transform (hence the name, "Fourier transform spectroscopy"). The raw data is sometimes called an "interferogram".

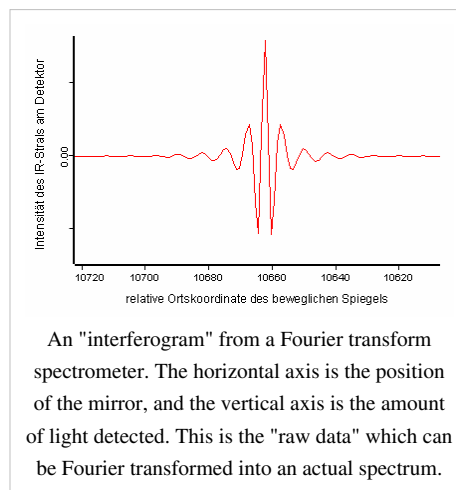


Measuring an absorption spectrum

The method of Fourier transform spectroscopy can also be used for absorption spectroscopy. The primary example is "FTIR Spectroscopy", a common technique in chemistry.

In general, the goal of absorption spectroscopy is to measure how well a sample absorbs or transmits light at each different wavelength. Although absorption spectroscopy and emission spectroscopy are different in principle, they are closely related in practice; any technique for emission spectroscopy can also be used for absorption spectroscopy. First, the emission spectrum of a broadband lamp is measured (this is called the "background spectrum"). Second, the emission spectrum of the same lamp *shining through the sample* is measured (this is called the "sample spectrum"). The sample will absorb some of the light, causing the spectra to be different. The ratio of the "sample spectrum" to the "background spectrum" is directly related to the sample's absorption spectrum.

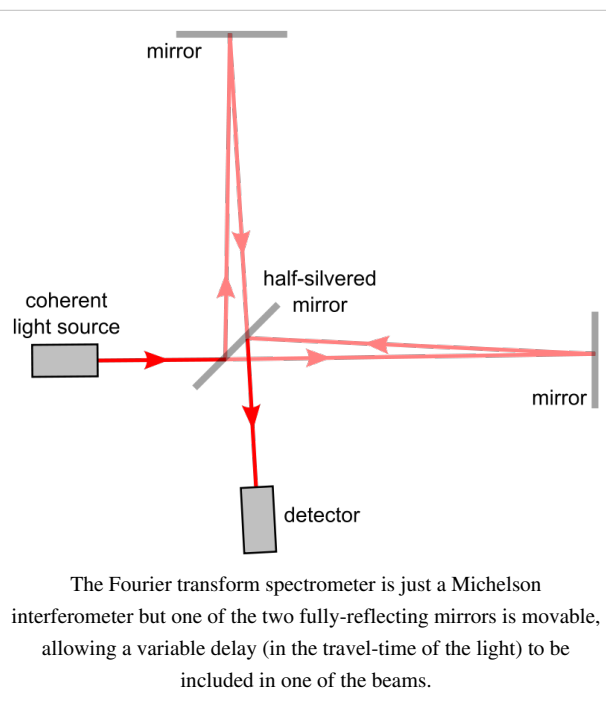
Accordingly, the technique of "Fourier transform spectroscopy" can be used both for measuring emission spectra (for example, the emission spectrum of a star), *and* absorption spectra (for example, the absorption spectrum of a glass of liquid).



Continuous wave *Michelson* or *Fourier transform* spectrograph

The Michelson spectrograph is similar to the instrument used in the Michelson-Morley experiment. Light from the source is split into two beams by a half-silvered mirror, one is reflected off a fixed mirror and one off a moving mirror which introduces a time delay—the Fourier transform spectrometer is just a Michelson interferometer with a movable mirror. The beams interfere, allowing the temporal coherence of the light to be measured at each different time delay setting, effectively converting the time domain into a spatial coordinate. By making measurements of the signal at many discrete positions of the moving mirror, the spectrum can be reconstructed using a Fourier transform of the temporal coherence of the light. Michelson spectrographs are capable of very high spectral resolution observations of very bright sources. The Michelson or Fourier transform spectrograph was popular for infra-red applications at a time when infra-red astronomy only had single pixel detectors.

Imaging Michelson spectrometers are a possibility, but in general have been supplanted by imaging Fabry–Pérot instruments which are easier to construct.



Fellgett advantage

One of the most important advantages of Fourier transform spectroscopy was shown by P.B. Fellgett, an early advocate of the method. The Fellgett advantage, also known as the multiplex principle, states that a multiplex spectrometer such as the Fourier transform spectroscopy will produce a gain of the order of the square root of m in the signal-to-noise ratio of the resulting spectrum, when compared with an equivalent scanning monochromator, where m is the number of elements comprising the resulting spectrum when the measurement noise is dominated by detector noise.

Converting spectra from time domain to frequency domain

$$S(t) = \int_{-\infty}^{\infty} I(\nu) e^{-i\nu 2\pi t} d\nu$$

The sum is performed over all contributing frequencies to give a signal $S(t)$ in the time domain.

$$I(\nu) = \int_{-\infty}^{\infty} S(t) e^{i\nu 2\pi t} dt$$

gives non-zero value when $S(t)$ contains a component that matches the oscillating function.

Remember that

$$e^{ix} = \cos x + i \sin x$$

See also

- Applied spectroscopy
- Forensic chemistry
- Forensic polymer engineering
- Nuclear Magnetic Resonance
- Infrared spectroscopy

External links

- Description of how a Fourier transform spectrometer works ^[4]
- The Michelson or Fourier transform spectrograph ^[5]
- Internet Journal of Vibrational Spectroscopy - How FTIR works ^[6]
- Fourier Transform Spectroscopy Topical Meeting and Tabletop Exhibit ^[7]

References

- [1] Antoine Abragam. 1968. *Principles of Nuclear Magnetic Resonance.*, Cambridge University Press: Cambridge, UK.
- [2] Peter Atkins, Julio De Paula. 2006. *Physical Chemistry*, 8th ed. Oxford University Press: Oxford, UK.
- [3] William H. Smith U.S. Patent 4976542 (<http://www.google.com/patents?vid=4976542>) Digital Array Scanned Interferometer, issued Dec. 11, 1990
- [4] <http://scienceworld.wolfram.com/physics/FourierTransformSpectrometer.html>
- [5] <http://www.astro.livjm.ac.uk/courses/phys362/notes/>
- [6] <http://www.ijvs.com/volume5/edition5/section1.html#Feature>
- [7] <http://www.osa.org/meetings/topicalmeetings/fts/default.aspx>

Nuclear magnetic resonance

Nuclear magnetic resonance (NMR) is a property that magnetic nuclei have in a magnetic field and applied electromagnetic (EM) pulse or pulses, which cause the nuclei to absorb energy from the EM pulse and radiate this energy back out. The energy radiated back out is at a specific resonance frequency which depends on the strength of the magnetic field and other factors. This allows the observation of specific quantum mechanical magnetic properties of an atomic nucleus. Many scientific techniques exploit NMR phenomena to study molecular physics, crystals and non-crystalline materials through NMR spectroscopy. NMR is also routinely used in advanced medical imaging techniques, such as in magnetic resonance imaging (MRI).

All stable isotopes that contain an odd number of protons and/or of neutrons (see Isotope) have an intrinsic magnetic moment and angular momentum, in other words a nonzero spin, while all nuclides with even numbers of both have spin 0. The most commonly studied nuclei are ^1H (the most NMR-sensitive isotope after the radioactive ^3H) and ^{13}C , although nuclei from isotopes of many other elements (e.g. ^2H , ^{10}B , ^{11}B , ^{14}N , ^{15}N , ^{17}O , ^{19}F , ^{23}Na , ^{29}Si , ^{31}P , ^{35}Cl , ^{113}Cd , ^{129}Xe , ^{195}Pt) are studied by high-field NMR spectroscopy as well.

A key feature of NMR is that the resonance frequency of a particular substance is directly proportional to the strength of the applied magnetic field. It is this feature that is exploited in imaging techniques; if a sample is placed in a non-uniform magnetic field then the resonance frequencies of the sample's nuclei depend on where in the field they are located. Since the resolution of the imaging techniques depends on how big the gradient of the field is, many efforts are made to develop more powerful magnets, often using superconductors. The effectiveness of NMR can also be improved using hyperpolarization, and/or using two-dimensional, three-dimensional and higher dimension multi-frequency techniques.



World's First 1 GHz NMR Spectrometer (1000 MHz, 23.5 T) was installed at the new 'Centre de RMN à Très Hauts Champs' in Lyon, France in August 2009



Pacific Northwest National Laboratory's high magnetic field (800 MHz, 18.8 T) NMR spectrometer.

The principle of NMR usually involves two sequential steps:

- The alignment (polarization) of the magnetic nuclear spins in an applied, constant magnetic field $\mathbf{H}_0$.
- The perturbation of this alignment of the nuclear spins by employing an electro-magnetic, usually radio frequency (RF) pulse. The required perturbing frequency is dependent upon the static magnetic field ($\mathbf{H}_0$) and the nuclei of observation.

The two fields are usually chosen to be perpendicular to each other as this maximizes the NMR signal strength. The resulting response by the total magnetization ($\mathbf{M}$) of the nuclear spins is the phenomenon that is exploited in NMR spectroscopy and magnetic resonance imaging. Both use intense applied magnetic fields ($\mathbf{H}_0$) in order to achieve dispersion and very high stability to deliver spectral resolution, the details of which are described by chemical shifts, the Zeeman effect, and Knight shifts (in metals).

NMR phenomena are also utilized in low-field NMR, NMR spectroscopy and MRI in the Earth's magnetic field (referred to as Earth's field NMR), and in several types of magnetometers.

History

Discovery

Nuclear magnetic resonance was first described and measured in molecular beams by Isidor Rabi in 1938,^[1] and in 1944, Rabi was awarded the Nobel Prize in physics for this work.^[2] In 1946, Felix Bloch and Edward Mills Purcell expanded the technique for use on liquids and solids, for which they shared the Nobel Prize in physics in 1952.^[3]

Purcell had worked on the development and radar applications during World War II at Massachusetts Institute of Technology's Radiation Laboratory. His work during that project on the production and detection of RF energy, and on the absorption of such RF energy by matter, preceded his discovery of NMR.

They noticed that magnetic nuclei, like ^1H and ^{31}P , could absorb RF energy when placed in a magnetic field of a strength specific to the identity of the nuclei. When this absorption occurs, the nucleus is described as being *in resonance*. Different atomic nuclei within a molecule resonate at different (radio) frequencies for the same magnetic field strength. The observation of such magnetic resonance frequencies of the nuclei present in a molecule allows any trained user to discover essential, chemical and structural information about the molecule.

The development of nuclear magnetic resonance as a technique of analytical chemistry and biochemistry parallels the development of electromagnetic technology and its introduction into civilian use.

Theory of nuclear magnetic resonance

Nuclear spin and magnets

All nucleons, that is neutrons and protons, composing any atomic nucleus, have the intrinsic quantum property of spin. The overall spin of the nucleus is determined by the spin quantum number S . If the number of both the protons and neutrons in a given nuclide are even then $S = 0$, i.e. there is no overall spin; just as electrons pair up in atomic orbitals, so do even numbers of protons or even numbers of neutrons (which are also spin- $\frac{1}{2}$ particles and hence fermions) pair up giving zero overall spin.

However, a proton and neutron will have lower energy when their spins are parallel, **not anti-parallel**, as this parallel spin alignment does not infringe upon the Pauli principle, but instead has to do with the quark structure of these two nucleons. Therefore, the spin ground state for the deuteron (the deuterium nucleus, or the ^2H isotope of hydrogen)—that has only a proton and a neutron—corresponds to a spin value of **1**, *not of zero*; the single, isolated deuteron is therefore exhibiting an NMR absorption spectrum characteristic of a quadrupolar nucleus of spin **1**, which in the 'rigid' state at very low temperatures is a characteristic ('Pake') *doublet*, (not a singlet as for a single, isolated ^1H , or any other isolated fermion or dipolar nucleus of spin $1/2$). On the other hand, because of the Pauli

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Spin behavior in a magnetic field

Consider nuclei which have a spin of one-half, like ^1H , ^{13}C or ^{19}F . The nucleus has two possible spin states: $m = \frac{1}{2}$ or $m = -\frac{1}{2}$ (also referred to as spin-up and spin-down, or sometimes α and β spin states, respectively). These states are degenerate, that is they have the same energy. Hence the number of atoms in these two states will be approximately equal at thermal equilibrium.

If a nucleus is placed in a magnetic field, however, the interaction between the nuclear magnetic moment and the external magnetic field mean the two states no longer have the same energy. The energy of a magnetic moment μ when in a magnetic field $\mathbf{B}_0$ is given by:

$$E = -\mu \cdot \mathbf{B}_0 = -\mu_x B_{0x} - \mu_y B_{0y} - \mu_z B_{0z}.$$

Usually the z axis is chosen to be along $\mathbf{B}_0$, and the above expression reduces to:

$$E = -\mu_z B_0,$$

or alternatively:

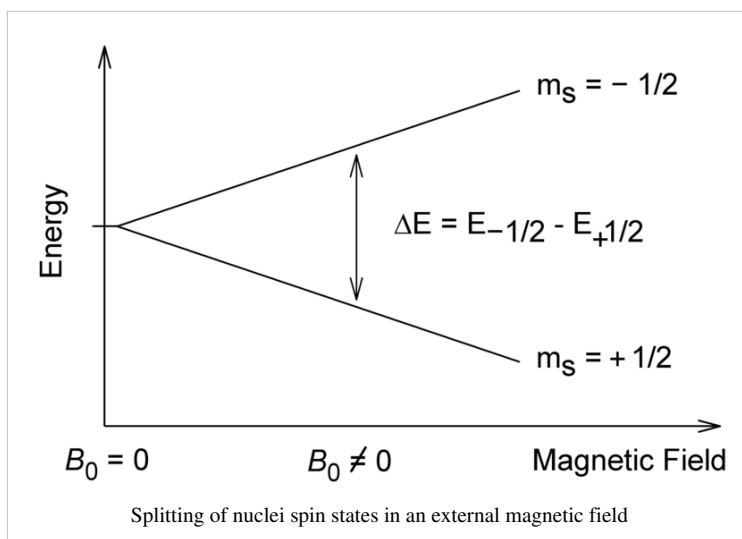
$$E = -\gamma \hbar B_0.$$

As a result the different nuclear spin states have different energies in a non-zero magnetic field. In hand-waving terms, we can talk about the two spin states of a spin $\frac{1}{2}$ as being *aligned* either with or against the magnetic field. If γ is positive (true for most isotopes) then $m = \frac{1}{2}$ is the lower energy state.

The energy difference between the two states is:

$$\Delta E = \gamma \hbar B_0,$$

and this difference results in a small population bias toward the lower energy state.



Magnetic resonance by nuclei

Resonant absorption by nuclear spins will occur only when electromagnetic radiation of the correct frequency (e.g., equaling the Larmor precession rate) is being applied to match the energy difference between the nuclear spin levels in a constant magnetic field of the appropriate strength. The energy of an absorbed photon is then $E = \hbar \nu_0$, where ν_0 is the resonance radiofrequency that has to match (that is, it has to be equal to) the Larmor precession frequency ν_L of the nuclear magnetization in the constant magnetic field $\mathbf{B}_0$. Hence, a magnetic resonance absorption will only occur when $\Delta E = \hbar \nu_0$, which is when $\nu_0 = \gamma B_0 / (2\pi)$. Such magnetic resonance frequencies typically correspond to the radio frequency (or RF) range of the electromagnetic spectrum for magnetic fields up to ~ 20 T. It is this magnetic resonant absorption which is detected in NMR.

Nuclear shielding

It might appear from the above that all nuclei of the same nuclide (and hence the same g) would resonate at the same frequency. This is not the case. The most important perturbation of the NMR frequency for applications of NMR is the 'shielding' effect of the surrounding electrons. In general, this electronic shielding reduces the magnetic field *at the nucleus* (which is what determines the NMR frequency).

As a result the energy gap is reduced, and the frequency required to achieve resonance is also reduced. This shift in the NMR frequency due to the electrons' molecular orbital coupling to the external magnetic field is called chemical shift, and it explains why NMR is able to probe the chemical structure of molecules which depends on the electron density distribution in the corresponding molecular orbitals. If a nucleus in a specific chemical group is shielded to a higher degree by a higher electron density of its surrounding molecular orbital, then its NMR frequency will be shifted "upfield" (that is, a lower chemical shift), whereas if it is less shielded by such surrounding electron density, then its NMR frequency will be shifted "downfield" (that is, a higher chemical shift).

Unless the local symmetry of such molecular orbitals is very high (leading to "isotropic" shift), the shielding effect will depend on the orientation of the molecule with respect to the external field ($\mathbf{B}_0$). In solid-state NMR spectroscopy, magic angle spinning is required to average out this orientation dependence in order to obtain values close to the average chemical shifts. This is unnecessary in conventional NMR investigations of molecules, since rapid molecular tumbling averages out the chemical shift anisotropy (CSA). In this case, the term "average" chemical shift (ACS) is used.

Relaxation

The process called population relaxation refers to nuclei that return to the thermodynamic state in the magnet. This process is also called T_1 , "spin-lattice" or "longitudinal magnetic" relaxation, where T_1 refers to the mean time for an individual nucleus to return to its thermal equilibrium state of the spins. Once the nuclear spin population is relaxed, it can be probed again, since it is in the initial, equilibrium (mixed) state.

The precessing nuclei can also fall out of alignment with each other (returning the net magnetization vector to a non-precessing field) and stop producing a signal. This is called T_2 or *transverse relaxation*. Because of the difference in the actual relaxation mechanisms involved (for example, inter-molecular vs. intra-molecular magnetic dipole-dipole interactions), T_1 is always longer than T_2 (that is, slower spin-lattice relaxation, for example because of smaller dipole-dipole interaction effects). In practice, the value of T_2^* which is the actually observed decay time of the observed NMR signal, or free induction decay, (to 1/e of the initial amplitude immediately after the resonant RF pulse)-- also depends on the static magnetic field inhomogeneity, which is quite significant. (There is also a smaller but significant contribution to the observed FID shortening from the RF inhomogeneity of the resonant pulse). In the corresponding FT-NMR spectrum—meaning the Fourier transform of the free induction decay--the T_2^* time is inversely related to the width of the NMR signal in frequency units. Thus, a nucleus with a long T_2 relaxation time gives rise to a very sharp NMR peak in the FT-NMR spectrum for a very homogeneous ("well-shimmed") static magnetic field, whereas nuclei with shorter T_2 values give rise to broad FT-NMR peaks even when the magnet is shimmed well. Both T_1 and T_2 depend on the rate of molecular motions as well as the gyromagnetic ratios of both the resonating and their strongly interacting, next-neighbor nuclei that are not at resonance.

NMR spectroscopy

NMR spectroscopy is one of the principal techniques used to obtain physical, chemical, electronic and structural information about molecules due to either the chemical shift, Zeeman effect, or the Knight shift effect, or a combination of both, on the resonant frequencies of the nuclei present in the sample. It is a powerful technique that can provide detailed information on the topology, dynamics and three-dimensional structure of molecules in solution and the solid state. Thus, structural and dynamic information is obtainable (with or without "magic angle" spinning (MAS)) from NMR studies of quadrupolar nuclei (that is, those nuclei with spin $S > \frac{1}{2}$) even in the presence of magnetic dipole-dipole interaction broadening (or simply, dipolar broadening) which is always much smaller than the quadrupolar interaction strength because it is a magnetic vs. an electric interaction effect.

Additional structural and chemical information may be obtained by performing double-quantum NMR experiments for quadrupolar nuclei such as ^2H . Also, nuclear magnetic resonance is one of the techniques that has been used to design quantum automata, and also build elementary quantum computers.^{[6] [7]}



900 MHz, 21.2 T NMR Magnet at HWB-NMR, Birmingham, UK

Continuous wave (CW) spectroscopy

In its first few decades, nuclear magnetic resonance spectrometers used a technique known as continuous-wave spectroscopy (CW spectroscopy). Although NMR spectra could be, and have been, obtained using a fixed magnetic field and sweeping the frequency of the electromagnetic radiation, this more typically involved using a fixed frequency source and varying the current (and hence magnetic field) in an electromagnet to observe the resonant absorption signals. This is the origin of the counterintuitive, but still common, "high" and "low" field terminology for low frequency and high frequency regions respectively of the NMR spectrum.

CW spectroscopy is inefficient in comparison to Fourier techniques (see below) as it probes the NMR response at individual frequencies in succession. As the NMR signal is intrinsically weak, the observed spectra suffer from a poor signal-to-noise ratio. This can be mitigated by signal averaging i.e. adding the spectra from repeated measurements. While the NMR signal is constant between scans and so adds linearly, the random noise adds more slowly—as the square-root of the number of spectra (see Random walk). Hence the overall ratio of the signal to the noise increases as the square-root of the number of spectra measured.

Fourier transform spectroscopy

Most applications of NMR involve full NMR spectra, that is, the intensity of the NMR signal as a function of frequency. Early attempts to acquire the NMR spectrum more efficiently than simple CW methods involved irradiating simultaneously with more than one frequency. A revolution in NMR occurred when short pulses of radio-frequency were used (centered at the middle of the NMR spectrum). In simple terms, a short square pulse of a given "carrier" frequency "contains" a range of frequencies centered about the carrier frequency, with the range of excitation (bandwidth) being inversely proportional to the pulse duration (the Fourier transform (FT) of an approximate square wave contains contributions from all the frequencies in the neighborhood of the principal frequency). The restricted range of the NMR frequencies made it relatively easy to use short (millisecond to microsecond) radiofrequency (RF) pulses to excite the entire NMR spectrum.

Applying such a pulse to a set of nuclear spins simultaneously excites all the single-quantum NMR transitions. In terms of the net magnetization vector, this corresponds to tilting the magnetization vector away from its equilibrium position (aligned along the external magnetic field). The out-of-equilibrium magnetization vector precesses about the external magnetic field vector at the NMR frequency of the spins. This oscillating magnetization vector induces a current in a nearby pickup coil, creating an electrical signal oscillating at the NMR frequency. This signal is known as the free induction decay (FID) and contains the vector-sum of the NMR responses from all the excited spins. In order to obtain the frequency-domain NMR spectrum (NMR absorption intensity vs. NMR frequency) this time-domain signal (intensity vs. time) must be FTed. Fortunately the development of FT NMR coincided with the development of digital computers and Fast Fourier Transform algorithms. FT methods can be applied to many types of spectroscopy; see the general article on Fourier transform spectroscopy.

Richard R. Ernst was one of the pioneers of pulse (FT) NMR and won a Nobel Prize in chemistry in 1991 for his work on FT NMR and his development of multi-dimensional NMR (see below).

Multi-dimensional NMR Spectroscopy

The use of pulses of different shapes, frequencies and durations in specifically-designed patterns or *pulse sequences* allows the spectroscopist to extract many different types of information about the molecule. Multi-dimensional nuclear magnetic resonance spectroscopy is a kind of FT NMR in which there are at least two pulses and, as the experiment is repeated, the pulse sequence is varied. In *multidimensional nuclear magnetic resonance* there will be a sequence of pulses and, at least, one variable time period. In three dimensions, two time sequences will be varied. In four dimensions, three will be varied.

There are many such experiments. In one, these time intervals allow (amongst other things) magnetization transfer between nuclei and, therefore, the detection of the kinds of nuclear-nuclear interactions that allowed for the magnetization transfer. Interactions that can be detected are usually classified into two kinds. There are *through-bond* interactions and *through-space* interactions, the latter usually being a consequence of the nuclear Overhauser effect. Experiments of the nuclear Overhauser variety may be employed to establish distances between atoms, as for example by 2D-FT NMR of molecules in solution.

Although the fundamental concept of 2D-FT NMR was proposed by Jean Jeener from the Free University of Brussels at an International Conference, this idea was largely developed by Richard Ernst who won the 1991 Nobel prize in Chemistry for his work in FT NMR, including multi-dimensional FT NMR, and especially 2D-FT NMR of small molecules.^[8] Multi-dimensional FT NMR experiments were then further developed into powerful methodologies for studying biomolecules in solution, in particular for the determination of the structure of biopolymers such as proteins or even small nucleic acids.^[9]

Kurt Wüthrich shared (with John B. Fenn) in 2002 the Nobel Prize in Chemistry for his work in protein FT NMR in solution.

Solid-state NMR spectroscopy

This technique complements biopolymer X-ray crystallography in that it is frequently applicable to biomolecules in a liquid or liquid crystal phase, whereas crystallography, as the name implies, is performed on molecules in a solid phase. Though nuclear magnetic resonance is used to study solids, extensive atomic-level biomolecular structural detail is especially challenging to obtain in the solid state. There is little signal averaging by thermal motion in the solid state, where most molecules can only undergo restricted vibrations and rotations at room temperature, each in a slightly different electronic environment, therefore exhibiting a different NMR absorption peak. Such a variation in the electronic environment of the resonating nuclei results in a blurring of the observed spectra—which is often only a broad Gaussian band for non-quadrupolar spins in a solid—thus making the interpretation of such "dipolar" and "chemical shift anisotropy" (CSA) broadened spectra either very difficult or impossible.

Professor Raymond Andrew at Nottingham University in the UK pioneered the development of high-resolution solid-state nuclear magnetic resonance. He was the first to report the introduction of the MAS (magic angle sample spinning; MASS) technique that allowed him to achieve spectral resolution in solids sufficient to distinguish between chemical groups with either different chemical shifts or distinct Knight shifts. In MASS, the sample is spun at several kilohertz around an axis that makes the so-called magic angle θ_m (which is $\sim 54.74^\circ$, where $\cos^2\theta_m = 1/3$) with respect to the direction of the static magnetic field $\mathbf{B}_0$; as a result of such magic angle sample spinning, the chemical shift anisotropy bands are averaged to their corresponding average (isotropic) chemical shift values. The above expression involving $\cos^2\theta_m$ has its origin in a calculation that predicts the magnetic dipolar interaction effects to cancel out for the specific value of θ_m called the magic angle. One notes that correct alignment of the sample rotation axis as close as possible to θ_m is essential for cancelling out the dipolar interactions whose strength for angles sufficiently far from θ_m is usually greater than ~ 10 kHz for C-H bonds in solids, for example, and it is thus greater than their CSA values.

There are different angles for the sample spinning relative to the applied field for the averaging of quadrupole interactions and paramagnetic interactions, correspondingly $\sim 30.6^\circ$ and $\sim 70.1^\circ$.

A concept developed by Sven Hartmann and Erwin Hahn was utilized in transferring magnetization from protons to less sensitive nuclei (popularly known as cross-polarization) by M.G. Gibby, Alex Pines and John S. Waugh. Then, Jake Schaefer and Ed Stejskal demonstrated also the powerful use of cross-polarization under MASS conditions which is now routinely employed to detect low-abundance and low-sensitivity nuclei.

Sensitivity

Because the intensity of nuclear magnetic resonance signals and, hence, the sensitivity of the technique depends on the strength of the magnetic field the technique has also advanced over the decades with the development of more powerful magnets. Advances made in audio-visual technology have also improved the signal-generation and processing capabilities of newer machines.

As noted above, the sensitivity of nuclear magnetic resonance signals is also dependent on the presence of a magnetically-susceptible nuclide and, therefore, either on the natural abundance of such nuclides or on the ability of the experimentalist to artificially enrich the molecules, under study, with such nuclides. The most abundant naturally-occurring isotopes of hydrogen and phosphorus (for example) are both magnetically susceptible and readily useful for nuclear magnetic resonance spectroscopy. In contrast, carbon and nitrogen have useful isotopes but which occur only in very low natural abundance.

Other limitations on sensitivity arise from the quantum-mechanical nature of the phenomenon. For quantum states separated by energy equivalent to radio frequencies, thermal energy from the environment causes the populations of the states to be close to equal. Since incoming radiation is equally likely to cause stimulated emission (a transition from the upper to the lower state) as absorption, the NMR effect depends on an excess of nuclei in the lower states. Several factors can reduce sensitivity, including

- Increasing temperature, which evens out the population of states. Conversely, low temperature NMR can sometimes yield better results than room-temperature NMR, providing the sample remains liquid.
- Saturation of the sample with energy applied at the resonant radiofrequency. This manifests in both CW and pulsed NMR; in the first, CW, case this happens by using too much continuous power that keeps the upper spin levels completely populated; in the second case, saturation occurs by pulsing too frequently—without allowing time for the nuclei to return to thermal equilibrium through spin-lattice relaxation. For nuclei such as ^{29}Si this is a serious practical problem as the relaxation time is measured in seconds; for protons in "pure" ice, or ^{19}F in high-purity (undoped) LiF crystals the spin-lattice relaxation time can be on the order of an hour or longer. The use of shorter RF pulses that tip the magnetization by less than 90° can partially solve the problem by allowing spectral acquisition without the complete loss of NMR signal.
- Non-magnetic effects, such as electric-quadrupole coupling of spin-1 and spin- $\frac{3}{2}$ nuclei with their local environment, which broaden and weaken absorption peaks. ^{14}N , an abundant spin-1 nucleus, is difficult to study for this reason. High resolution NMR instead probes molecules using the rarer ^{15}N isotope, which has spin- $\frac{1}{2}$.

Isotopes

Many chemical elements can be used for NMR analysis.^[10]

Commonly used nuclei:

- ^1H , the most commonly used spin $\frac{1}{2}$ nucleus in NMR investigation, has been studied using many forms of NMR. Hydrogen is highly abundant, especially in biological systems. It is the nucleus most sensitive to NMR signal (apart from ^3H which is not commonly used due to its instability and radioactivity). Proton NMR produces narrow chemical shift with sharp signals. The ^1H signal has been the sole diagnostic nucleus used for clinical magnetic resonance imaging.
- ^2H , a spin 1 nucleus commonly utilized as signal-free medium in the form of deuterated solvents during proton NMR, to avoid signal interference from hydrogen-containing solvents in measurement of ^1H solutes. Also used in determining the behavior of lipids in lipid membranes and other solids or liquid crystals as it is a relatively non-perturbing label which can selectively replace ^1H . Alternatively, ^2H can be detected in media specially labeled with ^2H .
- ^3He , is very sensitive to NMR. There is a very low percentage in natural helium, and subsequently has to be purified from ^4He . It is used mainly in studies of endohedral fullerenes, where its chemical inertness is beneficial to ascertaining the structure of the entrapping fullerene.
- ^{10}B , lower sensitivity than ^{11}B . Quartz tubes must be used as borosilicate glass interferes with measurement.
- ^{11}B , more sensitive than ^{10}B , yields sharper signals. Quartz tubes must be used as borosilicate glass interferes with measurement.
- ^{13}C spin- $\frac{1}{2}$, is widely used, despite its relative paucity in naturally-occurring carbon (approximately 1%). It is stable to nuclear decay. Since there is a low percentage in natural carbon, spectrum acquisition on samples which have not been experimentally enriched in ^{13}C takes a long time. Frequently used for labeling of compounds in synthetic and metabolic studies. Has low sensitivity and wide chemical shift, yields sharp signals. Low percentage makes it useful by preventing spin-spin couplings and makes the spectrum appear less crowded. Slow relaxation means that spectra are not integrable unless long acquisition times are used.
- ^{14}N , spin-1, medium sensitivity nucleus with wide chemical shift. Its large quadrupole moment interferes in acquisition of high resolution spectra, limiting usefulness to smaller molecules and functional groups with a high degree of symmetry such as the headgroups of lipids.
- ^{15}N , spin- $\frac{1}{2}$, relatively commonly used. Can be used for labeling compounds. Nucleus very insensitive but yields sharp signals. Low percentage in natural nitrogen together with low sensitivity requires high concentrations or expensive isotope enrichment.
- ^{17}O , spin- $\frac{5}{2}$, low sensitivity and very low natural abundance (0.037%), wide chemical shifts range (up to 2000 ppm). Quadrupole moment causing a line broadening. Used in metabolic and biochemical studies in studies of

chemical equilibria.

- ^{19}F , spin-1/2, relatively commonly measured. Sensitive, yields sharp signals, has wide chemical shift.
- ^{31}P , spin-1/2, 100% of natural phosphorus. Medium sensitivity, wide chemical shifts range, yields sharp lines.

Used in biochemical studies.

- ^{35}Cl and ^{37}Cl , broad signal. ^{35}Cl significantly more sensitive, preferred over ^{37}Cl despite its slightly broader signal. Organic chlorides yield very broad signals, its use is limited to inorganic and ionic chlorides and very small organic molecules.
- ^{43}Ca , used in biochemistry to study calcium binding to DNA, proteins, etc. Moderately sensitive, very low natural abundance.
- ^{195}Pt , used in studies of catalysts and complexes.

Other nuclei (usually used in the studies of their complexes and chemical binding, or to detect presence of the element):

- ^6Li , ^7Li
- ^9Be
- ^{19}F
- ^{21}Ne
- ^{23}Na
- ^{25}Mg
- ^{27}Al
- ^{29}Si
- ^{31}P
- ^{33}S
- ^{39}K , ^{40}K , ^{41}K
- ^{45}Sc
- ^{47}Ti , ^{49}Ti
- ^{50}V , ^{51}V
- ^{53}Cr
- ^{55}Mn
- ^{57}Fe
- ^{59}Co
- ^{61}Ni
- ^{63}Cu , ^{65}Cu
- ^{67}Zn
- ^{69}Ga , ^{71}Ga
- ^{73}Ge
- ^{77}Se
- ^{81}Br
- ^{87}Rb
- ^{87}Sr
- ^{95}Mo
- ^{109}Ag
- ^{113}Cd
- ^{119}Sn
- ^{125}Te
- ^{127}I
- ^{133}Cs
- ^{135}Ba , ^{137}Ba

- ^{139}La
- ^{183}W
- ^{199}Hg

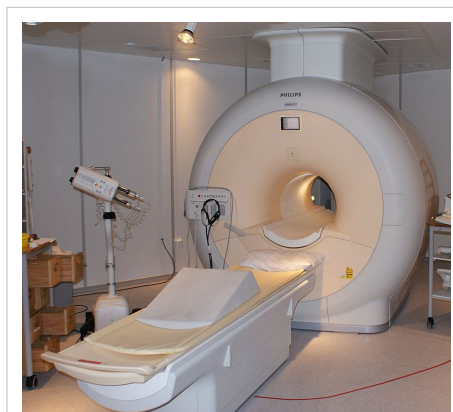
Applications

Medicine

The application of nuclear magnetic resonance best known to the general public is magnetic resonance imaging for medical diagnosis and MR Microscopy in research settings, however, it is also widely used in chemical studies, notably in NMR spectroscopy such as proton NMR, carbon-13 NMR, deuterium NMR and phosphorus-31 NMR. Biochemical information can also be obtained from living tissue (e.g. human brain tumors) with the technique known as *in vivo* magnetic resonance spectroscopy or chemical shift NMR Microscopy.

These studies are possible because nuclei are surrounded by orbiting electrons, which are charged particles that generate small, local magnetic fields that add to or subtract from the external magnetic field, and so will partially shield the nuclei. The amount of shielding depends on the exact local environment. For example, a hydrogen bonded to an oxygen will be shielded differently than a hydrogen bonded to a carbon atom. In addition, two hydrogen nuclei can interact via a process known as spin-spin coupling, if they are on the same molecule, which will split the lines of the spectra in a recognizable way.

As one of the two major spectroscopic techniques used in metabolomics, NMR is used to generate metabolic fingerprints from biological fluids to obtain information about disease states or toxic insults.



Medical MRI

Chemistry

By studying the peaks of nuclear magnetic resonance spectra, chemists can determine the structure of many compounds. It can be a very selective technique, distinguishing among many atoms within a molecule or collection of molecules of the same type but which differ only in terms of their local chemical environment. See the articles on carbon-13 NMR and proton NMR for detailed discussions.

By studying T_2^* information, a chemist can determine the identity of a compound by comparing the observed nuclear precession frequencies to known frequencies. Further structural data can be elucidated by observing *spin-spin coupling*, a process by which the precession frequency of a nucleus can be influenced by the magnetization transfer from nearby nuclei. Spin-spin coupling is most commonly observed in NMR involving common isotopes, such as Hydrogen-1 (^1H NMR).

Because the nuclear magnetic resonance *timescale* is rather slow, compared to other spectroscopic methods, changing the temperature of a T_2^* experiment can also give information about fast reactions, such as the Cope rearrangement or about structural dynamics, such as ring-flipping in cyclohexane. At low enough temperatures, a distinction can be made between the axial and equatorial hydrogens in cyclohexane.

An example of nuclear magnetic resonance being used in the determination of a structure is that of buckminsterfullerene (often called "buckyballs", composition C_{60}). This now famous form of carbon has 60 carbon atoms forming a sphere. The carbon atoms are all in identical environments and so should see the same internal H field. Unfortunately, buckminsterfullerene contains no hydrogen and so ^{13}C nuclear magnetic resonance has to be used. ^{13}C spectra require longer acquisition times since carbon-13 is not the common isotope of carbon (unlike hydrogen, where ^1H is the common isotope). However, in 1990 the spectrum was obtained by R. Taylor and

co-workers at the University of Sussex and was found to contain a single peak, confirming the unusual structure of buckminsterfullerene.^[11]

Non-destructive testing

Nuclear magnetic resonance is extremely useful for analyzing samples non-destructively. Radio waves and static magnetic fields easily penetrate many types of matter and anything that is not inherently ferromagnetic. For example, various expensive biological samples, such as nucleic acids, including RNA and DNA, or proteins, can be studied using nuclear magnetic resonance for weeks or months before using destructive biochemical experiments. This also makes nuclear magnetic resonance a good choice for analyzing dangerous samples.

Acquisition of dynamic information

In addition to providing static information on molecules by determining their 3D structures in solution, one of the remarkable advantages of NMR over X-ray crystallography is that it can be used to obtain important dynamic information including the low-frequency collective motion in proteins and DNA, for example in the Ca^{2+} -calmodulin system.^[12] The low-frequency internal motion in biomacromolecules and its biological functions have been discussed by Chou.^[13]

Data acquisition in the petroleum industry

Another use for nuclear magnetic resonance is data acquisition in the petroleum industry for petroleum and natural gas exploration and recovery. A borehole is drilled into rock and sedimentary strata into which nuclear magnetic resonance logging equipment is lowered. Nuclear magnetic resonance analysis of these boreholes is used to measure rock porosity, estimate permeability from pore size distribution and identify pore fluids (water, oil and gas). These instruments are typically low field NMR spectrometers.

Flow probes for NMR spectroscopy

Recently, real-time applications of NMR in liquid media have been developed using specifically designed flow probes (flow cell assemblies) which can replace standard tube probes. This has enabled techniques that can incorporate the use of high performance liquid chromatography (HPLC) or other continuous flow sample introduction devices.^[14]

Process control

NMR has now entered the arena of real-time process control and process optimization in oil refineries and petrochemical plants. Two different types of NMR analysis are utilized to provide real time analysis of feeds and products in order to control and optimize unit operations. Time-domain NMR (TD-NMR) spectrometers operating at low field (2–20 MHz for ^1H) yield free induction decay data that can be used to determine absolute hydrogen content values, rheological information, and component composition. These spectrometers are used in mining, polymer production, cosmetics and food manufacturing as well as coal analysis. High resolution FT-NMR spectrometers operating in the 60 MHz range with shielded permanent magnet systems yield high resolution ^1H NMR spectra of refinery and petrochemical streams. The variation observed in these spectra with changing physical and chemical properties is modeled using chemometrics to yield predictions on unknown samples. The prediction results are provided to control systems via analogue or digital outputs from the spectrometer.

Earth's field NMR

In the Earth's magnetic field, NMR frequencies are in the audio frequency range, or the very low frequency band of the radio frequency spectrum. Earth's field NMR (EFNMR) is typically stimulated by applying a relatively strong dc magnetic field pulse to the sample and, following the pulse, analyzing the resulting low frequency alternating magnetic field that occurs in the Earth's magnetic field due to free induction decay (FID). These effects are exploited in some types of magnetometers, EFNMR spectrometers, and MRI imagers. Their inexpensive portable nature makes these instruments valuable for field use and for teaching the principles of NMR and MRI.

Quantum computing

NMR quantum computing uses the spin states of molecules as qubits. NMR differs from other implementations of quantum computers in that it uses an ensemble of systems, in this case molecules. The ensemble is initialized to be the thermal equilibrium state (see quantum statistical mechanics).

Magnetometers

Various magnetometers use NMR effects to measure magnetic fields, including proton precession magnetometers (PPM) (also known as proton magnetometers), and Overhauser magnetometers. See also Earth's field NMR.

Makers of NMR equipment

Major NMR instrument makers include Oxford Instruments, Bruker, Spinlock SRL, General Electric, JEOL, Kimble Chase, Philips, Siemens AG and Varian, Inc..

See also

- Carbon-13 NMR
 - Chemical shift
 - Dynamic nuclear polarisation (DNP)
 - Earth's field NMR (EFNMR)
 - Free induction decay (FID)
 - In vivo magnetic resonance spectroscopy (MRS)
 - J-coupling
 - Larmor equation (Not to be confused with Larmor formula).
 - Larmor precession
 - Low field NMR
 - Magic angle spinning
 - Magnetometer
 - Magnetic resonance imaging (MRI)
 - NMR spectra database
 - NMR spectroscopy
 - NMR Microscopy
 - Nuclear magnetic resonance in porous media
 - Nuclear quadrupole resonance (NQR)
 - Protein dynamics
 - Protein NMR
 - Proton NMR
 - Rabi cycle
 - Relaxometry
-

- Relaxation (NMR)
- Solid-state NMR
- Zero field NMR

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External links

Tutorial

- NMR/MRI tutorial ^[17]
- NMR Library ^[18] NMR Concepts
- NMR Course Notes ^[19]

Animations and Simulations

- This animation shows a spin, the modification of spin with magnetic field and HF pulse, spin echo sequences, inversion recovery sequence, gradient echo sequence and relaxation of spin ^[20]
- Animation of NMR spin $\frac{1}{2}$ precession ^[21]
- A free interactive simulation of NMR principles ^[22]

Software

- CARA ^[23] - Computer Aided Resonance Assignment, freeware, developed at the group of Prof. Kurt Wüthrich
- CCPN ^[24] NMR software suite from community led Collaborative Computing Project for NMR.
- Janocchio ^[25] Conformation-dependent coupling and NOE prediction for small molecules.
- Mnova ^[26] - Multiplatform NMR processing, analysis and prediction software from Mestrelab Research ^[27].
- NMR processing software from ACD/Labs ^[28] for 1D ^[29] and 2D ^[30] NMR spectra. DB interface available.
- NMR Prediction software ACD/NMR Predictors ^[31]
- NMR simulation software QSim ^[32]
- Free software for simulation of spin coupled multiplets and DNMR spectra WINDNMR-Pro ^[33]
- NMR processing software NMRPipe ^[34]
- RMN ^[35] - An NMR data processing program for Macintosh Classic OS 9.
- SPINUS ^[36] website that uses neural networks to predict NMR spectra from chemical structures

Video

- introduction to NMR and MRI ^[37]
- Richard Ernst, NL - Developer of Multidimensional NMR techniques ^[38] Freeview video provided by the Vega Science Trust.
- 'An Interview with Kurt Wüthrich' ^[39] Freeview video by the Vega Science Trust (Wüthrich was awarded a Nobel Prize in Chemistry in 2002 "for his development of nuclear magnetic resonance spectroscopy for determining the three-dimensional structure of biological macromolecules in solution").

Wiki

- NMR Wiki ^[40] Open NMR,EPR,MRI web project
- NMR wiki in Chinese ^[41] Chinese NMR, MRI and EPR community

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- [16] <http://www.process-nmr.com/pdfs/NMR%20Overview.pdf>
- [17] <http://www.cis.rit.edu/htbooks/nmr/inside.htm>
- [18] <http://nmr.chinanmr.cn/guide/eNMR/eNMRindex.html>
- [19] <http://www.grandinetti.org/Teaching/Chem824/NMRNotes>
- [20] http://www.bigs.de/BLH/en/index.php?option=com_content&view=category&layout=blog&id=51&Itemid=222
- [21] <http://www.chem.queensu.ca/FACILITIES/NMR/nmr/webcourse/precess.htm>
- [22] <http://vam.anest.ufl.edu/forensic/nmr.html>
- [23] <http://cara.nmr.ch/>
- [24] <http://www.ccpn.ac.uk/>
- [25] <http://janocchio.sourceforge.net>
- [26] <http://mestrelab.com/products/mnova/details.html>
- [27] <http://mestrelab.com/>
- [28] <http://www.acdlabs.com/>
- [29] http://www.acdlabs.com/products/adh/nmr/1d_man/
- [30] <http://www.acdlabs.com/nmrworkbook>
- [31] http://www.acdlabs.com/products/adh/nmr/nmr_pred/

- [32] <http://www.bpc.lu.se/QSim>
- [33] <http://www.chem.wisc.edu/areas/reich/plt/windnmr.htm>
- [34] <http://spin.niddk.nih.gov/bax/software/NMRPipe>
- [35] <http://www.grandinetti.org/Software/RMN>
- [36] <http://www2.chemie.uni-erlangen.de/services/spinus/>
- [37] <http://www.youtube.com/watch?v=7aRKAXD4dAg>
- [38] <http://www.vega.org.uk/video/programme/21>
- [39] <http://www.vega.org.uk/video/programme/115>
- [40] <http://www.nmrwiki.org>
- [41] <http://wiki.chinanmr.cn>

NMR Spectroscopy

Nuclear magnetic resonance spectroscopy, most commonly known as **NMR spectroscopy**, is the name given to a technique which exploits the magnetic properties of certain nuclei. For details regarding this phenomenon and its origins, refer to the nuclear magnetic resonance article. The most important applications for the organic chemist are proton NMR and carbon-13 NMR spectroscopy. In principle, NMR is applicable to any nucleus possessing spin.

Many types of information can be obtained from an NMR spectrum. Much like using infrared spectroscopy (IR) to identify functional groups, analysis of a NMR spectrum provides information on the number and type of chemical entities in a molecule. However, NMR provides much more information than IR.

The impact of NMR spectroscopy on the natural sciences has been substantial. It can, among other things, be used to study mixtures of analytes, to understand dynamic effects such as change in temperature and reaction mechanisms, and is an invaluable tool in understanding protein and nucleic acid structure and function. It can be applied to a wide variety of samples, both in the solution and the solid state.



A 900MHz NMR instrument with a 21.2 T magnet at HWB-NMR, Birmingham, UK

Basic NMR techniques

When placed in a magnetic field, NMR active nuclei (such as ^1H or ^{13}C) absorb at a frequency characteristic of the isotope. The resonant frequency, energy of the absorption and the intensity of the signal are proportional to the strength of the magnetic field. For example, in a 21 tesla magnetic field, protons resonate at 900 MHz. It is common to refer to a 21 T magnet as a 900 MHz magnet, although different nuclei resonate at a different frequency at this field strength.

In the Earth's magnetic field the same nuclei resonate at audio frequencies. This effect is used in Earth's field NMR spectrometers and other instruments. Because these instruments are portable and inexpensive, they are often used for teaching and field work.

Chemical shift

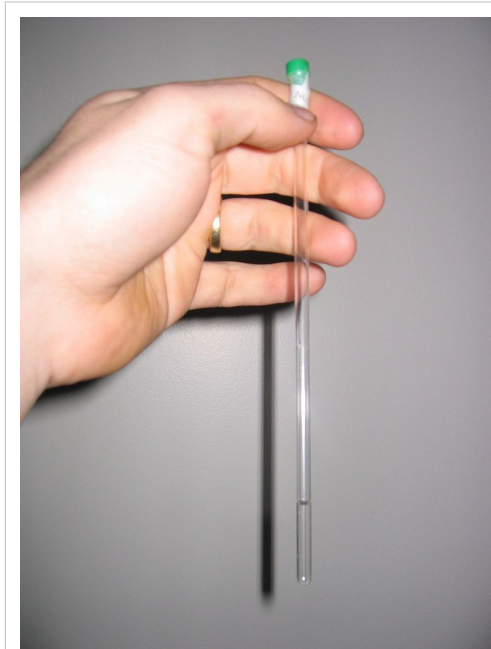
Depending on the local chemical environment, different protons in a molecule resonate at slightly different frequencies. Since both this frequency shift and the fundamental resonant frequency are directly proportional to the strength of the magnetic field, the shift is converted into a *field-independent* dimensionless value known as the chemical shift. The chemical shift is reported as a relative measure from some reference resonance frequency. (For the nuclei ^1H , ^{13}C , and ^{29}Si , TMS (tetramethylsilane) is commonly used as a reference.) This difference between the frequency of the signal and the frequency of the reference is divided by frequency of the reference signal to give the chemical shift. The frequency shifts are extremely small in comparison to the fundamental NMR frequency. A typical frequency shift might be 100 Hz, compared to a fundamental NMR frequency of 100 MHz, so the chemical shift is generally expressed in parts per million (ppm).^[1] To be able to detect such small frequency differences it is necessary, that the external magnetic field varies much less throughout the sample volume. High resolution NMR spectrometers use shims to adjust the homogeneity of the magnetic field to parts per billion (ppb) in a volume of a few cubic centimeters.

By understanding different chemical environments, the chemical shift can be used to obtain some structural information about the molecule in a sample. The conversion of the raw data to this information is called *assigning* the spectrum. For example, for the ^1H -NMR spectrum for ethanol ($\text{CH}_3\text{CH}_2\text{OH}$), one would expect three specific signals at three specific chemical shifts: one for the CH_3 group, one for the CH_2 group and one for the OH group. A typical CH_3 group has a shift around 1 ppm, a CH_2 attached to an OH has a shift of around 4 ppm and an OH has a shift around 2–3 ppm depending on the solvent used.

Because of molecular motion at room temperature, the three methyl protons *average* out during the course of the NMR experiment (which typically requires a few ms). These protons become degenerate and form a peak at the same chemical shift.

The shape and size of peaks are indicators of chemical structure too. In the example above—the proton spectrum of ethanol—the CH_3 peak would be three times as large as the OH. Similarly the CH_2 peak would be twice the size of the OH peak but only 2/3 the size of the CH_3 peak.

Modern analysis software allows analysis of the size of peaks to understand how many protons give rise to the peak. This is known as integration—a mathematical process which calculates the area under a graph (essentially what a spectrum is). The analyst must integrate the peak and not measure its height because the peaks also have *width*—and thus its size is dependent on its area not its height. However, it should be mentioned that the number of protons, or



The NMR sample is prepared in a thin-walled glass tube - an NMR tube.

any other observed nucleus, is only proportional to the intensity, or the integral, of the NMR signal, in the very simplest one-dimensional NMR experiments. In more elaborate experiments, for instance, experiments typically used to obtain carbon-13 NMR spectra, the integral of the signals depends on the relaxation rate of the nucleus, and its scalar and dipolar coupling constants. Very often these factors are poorly known - therefore, the integral of the NMR signal is very difficult to interpret in more complicated NMR experiments.

J-coupling

Multiplicity	Intensity Ratio
Singlet (s)	1
Doublet (d)	1:1
Triplet (t)	1:2:1
Quartet (q)	1:3:3:1
Quintet	1:4:6:4:1
Sextet	1:5:10:10:5:1
Septet	1:6:15:20:15:6:1

Some of the most useful information for structure determination in a one-dimensional NMR spectrum comes from **J-coupling** or **scalar coupling** (a special case of spin-spin coupling) between NMR active nuclei. This coupling arises from the interaction of different spin states through the chemical bonds of a molecule and results in the splitting of NMR signals. These splitting patterns can be complex or simple and, likewise, can be straightforwardly interpretable or deceptive. This coupling provides detailed insight into the connectivity of atoms in a molecule.

Coupling to n equivalent (spin $\frac{1}{2}$) nuclei splits the signal into a $n+1$ **multiplet** with intensity ratios following Pascal's triangle as described on the right. Coupling to additional spins will lead to further splittings of each component of the multiplet e.g. coupling to two different spin $\frac{1}{2}$ nuclei with significantly different coupling constants will lead to a *doublet of doublets* (abbreviation: dd). Note that coupling between nuclei that are chemically equivalent (that is, have the same chemical shift) has no effect on the NMR spectra and couplings between nuclei that are distant (usually more than 3 bonds apart for protons in flexible molecules) are usually too small to cause observable splittings. *Long-range* couplings over more than three bonds can often be observed in cyclic and aromatic compounds, leading to more complex splitting patterns.

For example, in the proton spectrum for ethanol described above, the CH_3 group is split into a *triplet* with an intensity ratio of 1:2:1 by the two neighboring CH_2 protons. Similarly, the CH_2 is split into a *quartet* with an intensity ratio of 1:3:3:1 by the three neighboring CH_3 protons. In principle, the two CH_2 protons would also be split again into a *doublet* to form a *doublet of quartets* by the hydroxyl proton, but intermolecular exchange of the acidic hydroxyl proton often results in a loss of coupling information.

Coupling to any spin $\frac{1}{2}$ nuclei such as phosphorus-31 or fluorine-19 works in this fashion (although the magnitudes of the coupling constants may be very different). But the splitting patterns differ from those described above for nuclei with spin greater than $\frac{1}{2}$ because the spin quantum number has more than two possible values. For instance, coupling to deuterium (a spin 1 nucleus) splits the signal into a *1:1:1 triplet* because the spin 1 has three spin states. Similarly, a spin $\frac{3}{2}$ nucleus splits a signal into a *1:1:1:1 quartet* and so on.

Coupling combined with the chemical shift (and the integration for protons) tells us not only about the chemical environment of the nuclei, but also the number of *neighboring* NMR active nuclei within the molecule. In more complex spectra with multiple peaks at similar chemical shifts or in spectra of nuclei other than hydrogen, coupling is often the only way to distinguish different nuclei.

Second-order (or strong) coupling

The above description assumes that the coupling constant is small in comparison with the difference in NMR frequencies between the inequivalent spins. If the shift separation decreases (or the coupling strength increases), the multiplet intensity patterns are first distorted, and then become more complex and less easily analyzed (especially if more than two spins are involved). Intensification of some peaks in a multiplet is achieved at the expense of the remainder, which sometimes almost disappear in the background noise, although the integrated area under the peaks remains constant. In most high-field NMR, however, the distortions are usually modest and the characteristic distortions (*roofing*) can in fact help to identify related peaks.

Second-order effects decrease as the frequency difference between multiplets increases, so that high-field (i.e. high-frequency) NMR spectra display less distortion than lower frequency spectra. Early spectra at 60 MHz were more prone to distortion than spectra from later machines typically operating at frequencies at 200 MHz or above.

Magnetic inequivalence

More subtle effects can occur if chemically equivalent spins (i.e. nuclei related by symmetry and so having the same NMR frequency) have different coupling relationships to external spins. Spins that are chemically equivalent but are not indistinguishable (based on their coupling relationships) are termed magnetically inequivalent. For example, the 4 H sites of 1,2-dichlorobenzene divide into two chemically equivalent pairs by symmetry, but an individual member of one of the pairs has different couplings to the spins making up the other pair. Magnetic inequivalence can lead to highly complex spectra which can only be analyzed by computational modeling. Such effects are more common in NMR spectra of aromatic and other non-flexible systems, while conformational averaging about C-C bonds in flexible molecules tends to equalize the couplings between protons on adjacent carbons, reducing problems with magnetic inequivalence.

Correlation spectroscopy

Correlation spectroscopy is one of several types of two-dimensional nuclear magnetic resonance (NMR) spectroscopy. This type of NMR experiment is best known by its acronym, COSY. Other types of two-dimensional NMR include J-spectroscopy, exchange spectroscopy (EXSY), Nuclear Overhauser effect spectroscopy (NOESY), total correlation spectroscopy (TOCSY) and heteronuclear correlation experiments, such as HSQC, HMQC, and HMBC. Two-dimensional NMR spectra provide more information about a molecule than one-dimensional NMR spectra and are especially useful in determining the structure of a molecule, particularly for molecules that are too complicated to work with using one-dimensional NMR. The first two-dimensional experiment, COSY, was proposed by Jean Jeener, a professor at Université Libre de Bruxelles, in 1971. This experiment was later implemented by Walter P. Aue, Enrico Bartholdi and Richard R. Ernst, who published their work in 1976.^[2]

Solid-state nuclear magnetic resonance

A variety of physical circumstances does not allow molecules to be studied in solution, and at the same time not by other spectroscopic techniques to an atomic level, either. In solid-phase media, such as crystals, microcrystalline powders, gels, anisotropic solutions, etc., it is in particular the dipolar coupling and chemical shift anisotropy that become dominant to the behaviour of the nuclear spin systems. In conventional solution-state NMR spectroscopy, these additional interactions would lead to a significant broadening of spectral lines. A variety of techniques allows to establish high-resolution conditions, that can, at least for ^{13}C spectra, be comparable to solution-state NMR spectra.

Two important concepts for high-resolution solid-state NMR spectroscopy are the limitation of possible molecular orientation by sample orientation, and the reduction of anisotropic nuclear magnetic interactions by sample spinning. Of the latter approach, fast spinning around the magic angle is a very prominent method, when the system comprises spin 1/2 nuclei. A number of intermediate techniques, with samples of partial alignment or reduced mobility, is

- Spectra library ^[18] NMR spectroscopy library
- Obtaining dihedral angles from ³J coupling constants ^[8]
- Another Javascript-like NMR coupling constant to dihedral ^[9]
- NMR Spectroscopy ^[10] Citizendium article on NMR Spectroscopy

Free NMR processing, analysis and simulation software

- WINDNMR-Pro ^[33] - simulation software for interactive calculation of first and second-order spin-coupled multiplets and a variety of DNMR lineshapes.
- CARA ^[11] - resonance assignment software developed at the Wüthrich group
- NMRShiftDB ^[12] - open database and NMR prediction website
- Spinworks ^[13]
- SPINUS ^[36] website that uses neural networks to predict NMR spectra from chemical structures
- MD-jeep ^[14] : free software for solving distance geometry problems related to NMR data

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